

REMARKS

The Office Action dated March 30, 2005, has been received and reviewed. Claims 32 and 34-35 are pending in the present application. Claims 32 and 34-35 stand rejected. Claim 35 has been canceled without prejudice or disclaimer. Applicants respectfully request reconsideration of the application in view of the arguments below.

I. Rejections under 35 U.S.C. § 102(b)

Applicants have canceled Claim 35 without prejudice or disclaimer thus mooting this rejection.

II. Rejections under 35 U.S.C. § 103(a)

Claims 32 and 24 stand rejected as allegedly being unpatentable by Huber et al., U.S. Patent No. 5,908,638 in view of Chesnut et al. (Metabolism Clinical and Experimental). Applicants respectfully traverse this rejection for the reasons discussed below.

To establish a *prima facie* case of obviousness, the prior art reference or references when combined must teach or suggest *all* the recitations of the claim, and there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). To support combining references, evidence of a suggestion, teaching, or motivation to combine must be clear and particular, and this requirement for clear and particular evidence is not met by broad and conclusory statements about the teachings of references. *In re Dembicza*k, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Court of Appeals for the Federal Circuit has also stated that, to support combining or modifying references, there must be particular evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Furthermore, as recently affirmed by the Court of Appeals for the Federal Circuit in *In re Sang-su Lee*, a factual

question of motivation is material to patentability, and cannot be resolved on subjective belief and unknown authority. See *In re Sang-su Lee*, 277 F.3d 1338 (Fed. Cir. 2002). Respectfully, as will be discussed below, the Official Action fails to meet the requirements for a *prima facie* showing of obviousness under § 103.

Applicants submit that Huber et al. does not teach or suggest Claims 32 and 34 of the present application. Huber et al. discloses the use of estrogens such as equilin, estrone, 17 α -dihydroequilin, 17 β -dihydroequilin and 17 α -estradiol and their corresponding sulfate esters. Huber et al. also discusses a composition containing a progestogen. However, Huber et al. fails to teach or suggest a composition consisting essentially of a mixture of estrogenic compounds wherein said mixture "comprises salts of conjugated estrone, conjugated equilin, conjugated $\Delta^{8,9}$ -dehydroestrone, conjugated 17 α -estradiol, conjugated 17 β -dihydroequilin, conjugated 17 α -dihydroequilin, conjugated 17 β -estradiol, conjugated equilenin, conjugated 17 α -dihydroequilenin, and conjugated 17 β -dihydroequilenin" and "therapeutically effective amount of a non-aromatizing androgenic compound". Huber et al. only disclose that "[a]ndrogens, such as testosterone and methyl testosterone are also contemplated as a combination with conjugated estrogens." Thus, there is no motivation to use Huber with any other reference.

Chestnut et al. similarly fails to teach or suggest all of the elements of the present invention. It also fails to teach or suggest a composition consisting essentially of a mixture of estrogenic compounds wherein said mixture "comprises salts of conjugated estrone, conjugated equilin, conjugated $\Delta^{8,9}$ -dehydroestrone, conjugated 17 α -estradiol, conjugated 17 β -dihydroequilin, conjugated 17 α -dihydroequilin, conjugated 17 β -estradiol, conjugated equilenin, conjugated 17 α -dihydroequilenin, and conjugated 17 β -dihydroequilenin" and "therapeutically effective amount of a non-aromatizing androgenic compound". Furthermore, Chestnut et al. was a study to evaluate total bone mass in patients. There is no suggestion or teaching that total bone mass has any overall effect on the health of the uterus. The present application illustrates data in an ovariectomized mouse model that demonstrates that estrogen/androgen therapy with an aromatizing androgen has a more detrimental effect on the uterus as evidenced by increased weight of the uterus than treatment with a non-aromatizing estrogen/androgen combination. This in turn leads to increased withdrawal bleeding which is disadvantageous. The combination of the salts of conjugated estrone, conjugated equilin, conjugated $\Delta^{8,9}$ -dehydroestrone, conjugated

17 α -estradiol, conjugated 17 β -dihydroequilin, conjugated 17 α -dihydroequilin, conjugated 17 β -estradiol, conjugated equilenin, conjugated 17 α -dihydroequilenin, and conjugated 17 β -dihydroequilenin" and "therapeutically effective amount of a non-aromatizing androgenic compound" as recited in the present claims is advantageous over what was previously known by one of skill in the art. Accordingly, because neither Huber et al. nor Chestnut et al. either teach or suggest alone or in combination the elements of the claims of the present application, Applicants submit that the claims in the pending application should be allowed. Applicants further submit that in view of the references and the above comments, that there was no motivation in either Huber et al. or Chestnut et al. to produce a composition consisting essentially of salts of conjugated estrone, conjugated equilin, conjugated $\Delta^{8,9}$ -dehydroestrone, conjugated 17 α -estradiol, conjugated 17 β -dihydroequilin, conjugated 17 α -dihydroequilin, conjugated 17 β -estradiol, conjugated equilenin, conjugated 17 α -dihydroequilenin, and conjugated 17 β -dihydroequilenin" and "therapeutically effective amount of a non-aromatizing androgenic compound" as recited in Claims 32 and 34.

CONCLUSION

In view of the remarks presented herein, Applicants respectfully submit that the claims define patentable subject matter. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

It is not believed that an extension of time and/or additional fee(s)-including fees for net addition of claims-are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that an extension of time is necessary to allow consideration of this paper, such an extension is hereby petitioned under 37 C.F.R. §1.136(a). Any additional fees believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully Submitted,



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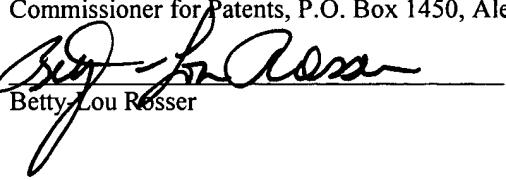
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